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PROFESSOR HISTOLOGY AND DERMATOLOGY

IN TOLEDO MEDICAL COLLEGE.

Read before the Northwestern Ohio Medical Association, at Van Wert, O., June 29, 1894.

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The essential histological elements of cancer consist of various forms of cells of epithelial character. The cells constitute larger or smaller spherical or elongated masses in alveolar or interstitial spaces of the part in which they grow. Accompanying ths growth of these cells, and the continuous penetration of them into such spaces, is an increase, more or less proportionate, of the fibrous tissue stroma.

In many cases the new tissue is, evidently, an inflammatory hyperplasia, produced by the irritating invasion of the epithelium. In other cases or forms, the stroma and vessels therein appear to be of new, embryonic formation, and while not of due proportion, as in surrounding tissues, yet not bearing evidence of inflammatory origin. Medullary or encephaloid, and the glandular varieties belong to this latter group, and scirrhous and epithelioma to the former. The cells filling the alveoli, to a greater or less degree, resemble normal epithelial forms found on such surfaces, or in such masses where the growth originated. Conditions of rapid growth, of age, of degenerative changes, and of pressure, determine the shape, size and other attributes of the cells.

If the theory or hypothesis rather, of Cohnheim, that tumors arise from the inclusion of embryonic cells or collections of cells, which, after complete evolution of the tissues, are by some stimulus excited to growth and development, unrestrained and undirected by co-ordinate or co-operative growth and development of the whole—if this be true, which seems not improbable, then the embryonic cells or bits of tissue from which the carcinomata arise, must have undergone evolution up to the stage of differentiation of the germinal layers In fact this must be true also of all tumor pathogenesis, except, perhaps, for the so-called "dermoid cysts." For, leaving out these last, we find no abstractly

heterologous tumors; but those of mesoblastic character taking rise from tissue of mesoblastic origin, and the epithelial from hypo- and epiblastic sites only.

What a matter of interest, perhaps of conjecture only, to look down along the path of tissue evolution, to see where nature's emigration train has, unnoticed, dropped the undeveloped, imperfect seed here and there along the way, to lie unseen, perchance to spring into luxuriant and noxious growth long afterwards.

Away down in the scale of development, probably from among the mass of cells, having common and undifferentiated protencies, was left aside from the current of evolution's tide a cell or two, before the germinal layers had begun to form. From these we get all sorts of tissues, epithelial and mesoblastic, in the "dermoid cyst." Further up, where the ways divide apart, we have the separation into three classes of cells, and across the line our growths cannot pass, but just this side of the line we have those abandoned orphans of nature who have all the possibilities of the mesoblast in its infancy.

Here the sarcomata spring, up; and so on, and on, coming down to those which must have been passed by, just before the final completion of tissue, to give rise to tumors much like the normal forms. Curiously enough, we get no true nervous tissue tumer growth, except in "dermoids" and the sustentacular tissue, neurogliar gliomata.

So these cancerous tumors also show their ancestral traits, for, not only do they arise from epithelial structures solely, but they exhibit in morphology a similarity, more or less distinctly expressed, to the epithelium of the organ or surface, in which their parent cell was included. Thus, the epitheliomata of epidermic origin have more or less squamous cells, as also the more massive and even semi-columnar ones, which show degenerative changes similar to stratum corneum, lucidum and the malpighian layer. Cells like those in concentric nests and "pearls" staining like similar cells in stratum lucidum and corneum. Those of internal passages, of hypoblastic deriviation have cells of columnar form with other distorted shapes. So, also, those of glandular site present forms similar to those of the mature gland, or to those of general embryonic gland form.

The development of normal cells, from the oösperm through all its progeny up to the fully matured individual living organism, show a purposive tendency, a disposition even through many metamorphoses to arrive at definate and orderly complexity and differentiation. And, if abortive and monstrous forms occur, they are from interrupted and incomplete development, or some diversion of evolution into long obsolete but primeval paths. That is to say, however diverse the outcome of development may be, from that which now constitutes the complete and perfected structures or organism, the resultant parts or whole, show the

attempt of the injured, hindered or exuberant cell to develop along the lines, and to the ends shaped by ancestral environment. Therefore, we are justified in believing that these pathological forms are attempts of the aroused embryonic cell (hitherto latent), to produce something which it might have completed, had it gone on in tissue construction aided and restrained by its fellows.

Of epithelial tumor construction we have at the extreme two classes, one which is nearer maturity in embryonic ancestry, and therefore the main line—the benign adenomata, which frequently, in its more perfect forms, rather closely resembles normal glands in structure and function—that is, producing something resembling some of the glandular secretions. These may be set down as the epithelial analogues of the more mature varieties of mesoblastic tumor formation—the benign fibro-, lipo-, chondro-, osteo-, myomata, etc. At the other extreme are the carcinomata; these are for the most part made up, as previously stated, of masses of epitheloid cells, penetrating into the adjacent tissues. These may be classed as of the "cadet" line, which left the train of evolution farther back, and not having received the directing and restraining impress of orderly developement and association as late as the other class, produce more aberrant forms. These are analogous to the malignant mesoblastic tumors—those embryonic and immature-featured sarcomata.

In the sarcomata we recognize the mesoblastic tissue tendencies as much as in those of maturer and more stable development. So it seems to me we may recognize in the carcinomata the tendency to gland production, even though lacking most essentials of the adult organ.

Epiblastic glands are developed by the ingrowth of solid cylinders of epithelial cells, which branch and ramify or remain more simple, with formation of lumen in ducts and acini by separation or degenerative solution and mingling in first secretion; further there is formed the specialized limiting basement membrane, continuous with that which lies beneath the malpighian layer, and upon the vascular corium.

In hypoblastic gland evolution, in some cases the same process obtains, but many of the glands are produced by tubular involutions of the mesenteron with subsequent specialization of cells into gland epithelium. These invaginations may remain as simple tubular glands or become complex. The adenomata originate in the same manner, and some of them having lumena with cystic exaggeration, while others persist as solid cylinders of epithelium.

As before said, the more perfect the approximation to normal type, the more benign their characteristics. But these epithelial new growths are not all benign, many of them having distinctly glandular appearance, being quite malignant. Now, these go over toward the border line of carcinomata, and not only is there a shading off of the

adenomata and carcinomata toward each other in quality, but also in optical appearance. And this insensible graduation goes on clear through the epithelial tumor growths from one extreme to the other.

At the extreme of carcinomata, we have the attempt at the production of gland tissue, but it reaches only the earlier embryonic stage in that line of evolution; that is, the ingrowth of epithelial or epitheloid cells in alveolar or cylindrical masses, without orderly arrangement, the formation of lumen or membrana propria.

While the most embryonic of sarcomas, those consisting of granulation cell elements, are recognized as abortive attempts at connective tissue construction, these epithelial ingrowths have been classed as "anomalous" instead of being denominated as of the type of "embryonic adenomatous tissue" tumors. For such they properly should be.

The general arrangement of cancerous growths and the cell peculiarities have, without a doubt, something of ontogenous impress; that is, are inffnenced in this way by the characteristics of contiguous structures. We see this quite markedly in the sarcomata, which take on pigmentary; or reticular, or alveolar form, if growing near or into structures having these qualities. Nevertheless, the phylogenous influence, or that of ancestral cell acquirement is the major one, for these growths never pass over the line which has differentiated the mesoblastic from the epithelial, thus exemplifying the laws of the "instability of the homogenous" and "of increasing heterogenity," long ago recognized by Von Baer and Herbert Spencer. For, though we find many examples of tumors taking on appearances in greator or less mimicry of contiguous tissues, we have every year more convincing evidence that the invasion of tumors by peripheral extension or embolic implantation in tissues of a specifically different class, has no effect to render its histogenesis other than that produced by that of ancestral or phylogenous impress.

The primary site of cancer, remote from some glandular structure, is in the nature of things almost an imposibility, except, perhaps, those arising from the so-called endothelial surfaces as the serious body-cavities. So that the phylogenous influences in cancer are not so readily distinguishable from those strictly ontogenous.

In tumors of mesoblastic type it is, in very many cases, much more readily observed, for while many are decidedly homeotopic, the heterotopic forms are perhaps quite as frequent. The lymph-adenomatous structure, and the pigmented varieties of sarcomata, when originating in or near normal tissues having such features, are undoubted examples of local influence. Growths of fat, fibrous tissue, muscle, etc., in like normal tissue sites, are probably examples of late developmental interruption of the cells of origin. Heterotopic growths as of bone, cartilage, fat and muscle, whether benign (and therefore of more mature type), or malignant, (and therefore more embryonic) necessarily must be interpreted as

exhibiting some directing influence other than that of contiguous normal tissues.

Microscopical investigations in histology, embryology and pathology, have demonstrated that in pathogenesis, as in normal histogenesis, there is, we may say, a determinate effort toward orderly and definite development. But the immediate cell ancestors of cancer growth, as of other neoplasms, lack the restraining and co-ordinating impress of the later stages of tissue evolution. The necessary exuberance of growth and deficient stability, as well as the time of appearance, verifying for this much at least, the aphorism of Virchow, that "disease processes consist in excess, or deficiency, or being at the wrong time, or the wrong place."